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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,123	10/09/2001	Scott M. Evans	[illegible]	[illegible]

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/975,123	Freier
Examiner	**Art Unit**
Jane Zara	1635

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Jan 22, 2003*.

2a) This action is **FINAL.** 2b) X This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-10 and 12-15* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *1-10 and 12-15* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

1. Notice of References Cited (PTO-892)
2. Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. Information Disclosure Statement(s) (PTO-1449) Paper No(s).
5. Notice of Informal Patent Application (PTO-152)

DETAILED ACTION

This Office action is in response to the communication filed January 22, 2003, Paper No. 6.

Claims 1-10, 12-15 are pending in the instant application.

Any rejections not repeated in this Office action are hereby withdrawn.

Response to Arguments and Amendments

Maintained Rejections

Claims 1-5, 11-19 are rejected under 35 U.S.C. 102(a) as being anticipated by Miyake et al.

Miyake et al (WO 01/05435 A2) teach the in vitro administration of compositions comprising antisense oligonucleotides which specifically target an active site on the nucleic acid encoding mIGF-BP5, and inhibit the expression of the nucleic acid encoding mIGF-BP5 in target cells in vitro, and which compositions further comprise a colloidal dispersion and a pharmaceutical compatible diluent, and which antisense comprise phosphorothioate internucleotide linkages. Miyake et al teach the intraperitoneal administration of compositions comprising an antisense oligonucleotide between 8 and 50 nucleobases in length which specifically targets mIGF-BP5 and inhibits its expression in vitro and in tumor cells in mice (a prostate related mouse model system).

comprises phosphorothioate internucleotide linkages, whereby tumor reduction is observed

following the administration of antisense to the mice (See entire document, especially figures 1-6, 8-10; also see accompanying nucleic acid sequence alignments between SEQ ID NO: 14 and AAA91253 of Miyake; SEQ. ID NO: 16 and AAA91241 of Miyake; SEQ ID NO: 17 and AAA91240 of Miyake; SEQ ID NO: 19 and AAA91239 of Miyake; SEQ ID NO: 21 and AAA91202 of Miyake; SEQ Id NO: 25 and AAA91203 of Miyake).

No arguments have been made addressing this rejection.

New Rejections and Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 1, the metes and bounds of the term "compound" cannot be determined. Appropriate clarification is requested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making

Claims 1-10, 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The term "intro/exon junction region" is not in the specification. Applicants argue that the specification supports the amendments to the claims that recite this term (referring to pages 83-85 of the specification). These pages indicated do not describe the term "inton/exon junction region". SEQ ID NO: 11 comprises 21,000 nucleobases, and the instant specification describes a single intron/exon junction sequence in Table 1, page 85. Nowhere are intron/exon junction regions described. Accordingly, the term "intron/exon junction region" constitutes new matter.

The claims are drawn to compositions and methods comprising the administration of antisense oligonucleotides targeted to intron or intron/exon junction regions of a nucleic acid encoding insulin like growth factor binding protein 5 (ILGFBP 5) of SEQ ID NO: 11.

The specification and claims do not adequately describe the distinguishing attributes concisely shared by the members of the genus comprising intro exon junction regions of SEQ ID NO: 11. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. Since the disclosure fails to describe the attributes concisely identifying members of the proposed genus (i.e. sequences

comprises 21,000 nucleobases, and the instant specification describes a single intron exon junction

sequence in Table 1, page 85. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number species to describe the genus claimed, drawn to any and/or all intron/exon junction regions within the 21,000 nucleobase sequence of SEQ ID NO: 11.

Claims 1 10, 12 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions and methods for inhibiting the expression of (ILGFBP 5) of SEQ ID NO: 3 or 10 in vitro comprising the administration of antisense oligonucleotides, does not reasonably provide enablement for inhibiting ILGFBP 5 comprising the administration of antisense oligonucleotides that target any and/or all intron/exon junction regions of SEQ ID NO: 11, nor is it enabling for the ex vivo administration of antisense which target and inhibit the expression of ILGFBP 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to compositions and methods comprising the administration of antisense oligonucleotides targeted to intron or intron exon junction regions of a nucleic acid encoding insulin like growth factor binding protein 5 (ILGFBP 5) of SEQ ID NO: 11. The claims are drawn to compositions and methods comprising the ex vivo administration of antisense oligonucleotides targeted to nucleic acid encoding insulin like growth factor binding protein 5

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of inhibiting the expression of ILGFBP 5 comprising the administration of antisense that target any and/or all intron/exon junction regions of SEQ ID NO: 11. Applicants have not provided adequate guidance describing any and/or all intron/exon junction regions of SEQ ID NO: 11. Furthermore, applicants have not provided guidance in the specification for the ex vivo administration of of antisense which target ILGFBP 5 *(If, in claim 15, the term --in vitro-- were inserted into the preamble of the claim, this would perhaps overcome the scope rejection addressing ex vivo applications).*

SEQ ID NO: 11 comprises 21,000 nucleobases, and the instant specification describes a single intron/exon junction sequence in Table 1, page 85. The listing of a single intron/exon junction sequence within SEQ ID NO: 11 is not representative or correlative of any and/or all intron/exon junction regions within SEQ ID NO: 11. In addition, the specification teaches the in vitro inhibition of expression of hILGFBP 5 encoded by Seq ID Nos: 3 or 10 comprising antisense oligonucleotides targeting these sequences. One skilled in the art would not accept on its face the examples given in the specification of the in vitro inhibition of expression of hILGFBP 5 of SEQ ID NO: 3 or 10 as being correlative or representative of the ex vivo administration of antisense, whereby target gene inhibition is demonstrated upon administration of antisense

that organism. Nor are these examples representative or correlative of the successful description

of any and/or all exon/intron junction regions of SEQ ID NO: 11, or of inhibition of expression of ILGFBP 5 in vitro comprising the targeting of these regions in view of the lack of guidance in the specification and unpredictability associated with the ability to predict the sequences comprising any and/or all inton/exon junction regions of ILGFBP 5. The specification as filed fails to provide any particular guidance which resolves the known unpredictability in the art associated with determination and adequate description of the sequences comprising any and/or all intron/exon junction regions of SEQ ID NO: 11.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to compositions and methods comprising the administration in vitro and ex vivo of antisense oligonucleotides targeted ILGFBP 5, and to intron or intron/exon junction regions of a nucleic acid encoding (ILGFBP 5) of SEQ ID NO: 11. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites comprising any and/or all intron/exon junction regions of SEQ ID NO: 11, whereby ILGFBP 5 expression is inhibited in vitro, as well as require the de novo determination of the ability to administer transfected cells back into an organism, whereby target gene inhibition is successfully demonstrated in that organism. Since the specification fails to provide any particular guidance for the successful inhibition of expression of ILGFBP 5 in vitro or ex vivo comprising administration of antisense which target ILGFBP 5, and

factors is highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

April 4, 2003

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PATENT EXAMINER